FACSIMILE COVER SHEET

Fax: 352-3725800

SALIWANCHIK, LLOYD & SALIWANCHIK

A Professional Association P.O. Box 142950 Gainesville, FL 32614-2950

> Telephone (352) 375-8100 Facsimile (352) 372-5800

TO:

Examiner Ilia I. Ouspenski

FROM:

Frank C. Eisenschenk, Ph.D.

COMPANY:

U.S. Patent Office

DATE:

July 30, 2010

FAX NO.:

571-273-2920

NUMBER OF PAGES

(INCLUDING COVER SHEET):

SUBJECT/MESSAGE:

Re:

U.S. Patent Application Docket No. ISI.103

RECEPTOR MODULATORS

(Davis)

Serial No. 10/585,491; filed July 7, 2006

Dear Examiner Ouspenski: In accordance with your request, attached is page 9 of the Amendment dated July 16, 2010.

The information contained in this facsimile message is intended only for the personal and confidential use of the designated recipients named above. This message may be an attorney-client communication, and as such is privileged and confidential. If the reader of this message is not the intended recipient or an agent responsible for delivering it to the intended recipient, you are hereby notified that you have received this document in error, and that any review, dissemination, distribution, or copying of this message is strictly prohibited. If you have received this communication in error, please notify us immediately by telephone and return the original message by mail. Thank you

If you do not receive all pages or if any transmission is not legible, call the sender at (352) 375-8100.

9

Docket No. ISI.103 Serial No. 10/585,491

antibodies to PD-1 is restricted to the sequence LAAFPEDRSQPGQDCR (SEQ ID NO: 61) and the Office Action provides no evidence that the antibodies made to this sequence would be expected to bind to epitopes containing amino acids other than this specific sequence (e.g., discontinuous epitopes containing the sequence). Applicant also notes that antibodies that bind to only this sequence are also outside the scope of the claims.

Applicant further notes that the substitution of a single amino acid in the sequence of a protein is sufficient to render the protein resistant to binding (neutralization) by both polyclonal and monoclonal antibodies. For example, Watkins et al. (attached with this response) clearly demonstrate that single and double mutations in the sequence of HIV-1 envelope protein abrogate antibody binding to, and neutralization of, HIV-1 and that a single amino acid mutation is sufficient to alter the conformation of the polypeptide such that antibodies do not bind to the protein at multiple epitopes (see Abstract and page 8436, last paragraph). Indeed, Watkins et al. indicate that numerous studies have illustrated how changes in one region of a protein produce alterations in noncontiguous regions of that protein. In this case, it is unclear how antibodies that were generated against the LAAFPEDRSQPGQDCR (SEQ ID NO: 61) peptide would be expected to bind to an epitope comprising PALLVV (SEQ ID NO: 44) or an epitope comprising SEQ ID NO: 61 (e.g., a discontinuous epitope containing SEQ ID NO: 61) since Hunig et al. fail to teach the production of antibodies to such an epitope and those skilled in the art would have known that changes in the amino acid sequence of the epitope to which the antibody was raised would have reasonably been expected to abrogate antibody binding. Accordingly, reconsideration and withdrawal of the rejection set forth over Hunig et al. is respectfully requested.

Turning, next, to the rejection over Wood et al., Applicant respectfully submits that this reference also fails to teach or anticipate the claimed antibody. While Applicant acknowledges that "the discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer" (Atlas Powder Co. v. Ireco Inc., 190 F.3d 1342, 1347, 51 USPQ2d 1943, 1947 (Fed. Cir. 1999)), Applicant also notes that, in order to anticipate, a prior art reference must also provide an enabling disclosure of the desired subject matter; mere naming or description of the subject matter is insufficient, if it cannot be produced without undue experimentation. Elan Pharm., Inc. v. Mayo

J:\\S\\103\Amd-Resp\Amd,doc/DNB/jb